

# EXHIBIT 1

Blood. 1999 Apr 1;93(7):2267-73.

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## **Antifactor VIII antibody inhibiting allogeneic but not autologous factor VIII in patients with mild hemophilia A.**

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Two unrelated patients with the same Arg2150His mutation in the factor VIII (FVIII) C1 domain, a residual FVIII activity of 0.09 IU/mL, and inhibitor titres of 300 and 6 Bethesda Units, respectively, were studied. Further analysis of patient LE, with the highest inhibitor titer, showed that (1) plasma or polyclonal IgG antibodies prepared from LE plasma inhibited the activity of allogeneic (wild-type) but not of self FVIII; (2) the presence of von Willebrand factor (vWF) increased by over 10-fold the inhibitory activity on wild-type FVIII; (3) the kinetics of FVIII inhibition followed a type II pattern, but in contrast to previously described type II inhibitors, LE IgG was potentiated by the presence of vWF instead of being in competition with it; (4) polyclonal LE IgG recognized the FVIII light chain in enzyme-linked immunosorbent assay and the recombinant A3-C1 domains in an immunoprecipitation assay, indicating that at least part of LE antibodies reacted with the FVIII domain encompassing the mutation site; and (5) LE IgG inhibited FVIII activity by decreasing the rate of FVIIIa release from vWF, but LE IgG recognized an epitope distinct from ESH8, a murine monoclonal antibody exhibiting the same property. We conclude that the present inhibitors are unique in that they clearly distinguish wild-type from self, mutated FVIII. The inhibition of wild-type FVIII by LE antibody is enhanced by vWF and is associated with an antibody-dependent reduced rate of FVIIIa release from vWF.

### Publication Types:

- **Case Reports**

PMID: 10090936 [PubMed - indexed for MEDLINE]